<International Research Center for Elements Science> Organic Main Group Chemistry

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Scope of Research

Our research activity is focused on the discovery, design and development of new molecular transformation reactions, which can provide new ways of efficient exploitation of chemical resources, such as haloalkanes, alkenes, alcohol etc. The present research subjects are (1) 3d-transition metal catalyzed controlled Carbon–Carbon bond forming reactions which exploit universal metals such as iron, magnesium and aluminum (2) understanding and design of synergistic effects of multi-element center interactions for the catalysis with the help of quantum chemical methods.

Research Activities (Year 2007)

Publications

Endo K, Hatakeyama T, Nakamura M, Nakamura E: Indium-Catalyzed 2-Alkenylation of 1,3-Dicarbonyl Compounds with Unactivated Alkynes, *J. Am. Chem. Soc.*, **129**, 5264-5271 (2007).

Hatakeyama T, Nakamura M: Iron-Catalyzed Selective Biaryl Coupling: Remarkable Suppression of Homocoupling by the Fluoride Anion, *J. Am. Chem. Soc.*, **129**, 9844-9845 (2007).

Tsuji H, Yamagata K-i, Itoh Y, Endo K, Nakamura M, Nakamura E: Indium-Catalyzed Cycloisomerization of ω-Alkynyl-β-ketoesters into Six- to Fifteen-Membered Rings, *Angew. Chem. Int. Ed.*, **46**, 8060-8062 (2007).

Presentations

Nakamura M, Asian Core Program (ACP) Lectureship Tour in Hong Kong (Chinese University of Hong Kong, Hong Kong Baptist University, Hong Kong University of Science and Technology, The University of Hong Kong), February 2007.

Nakamura M, The 99th National Meeting of Korean Chemical Society, Seoul, Korea, April 2007.

Nakamura M, ACP Lectureship tour in China, Shanghai Institute of Organic Chemistry, Fudan University, Shanghai Institute of Chemistry, Chinese Academy of Science, Beijing, China, May 2007.

Grants

Nakamura M, Development of Iron Catalyzed Reaction for Transformation of Polyvinylchloride, Grant-in-Aid for Exploratory Research, 1 April 2005–31 March 2007.

Nakamura M, Molecular Transformation of Unreactive Haloalkanes, Grant-in-Aid for Scientific Research on Priority Areas, 1 April 2006–31 March 2007.

Nakamura M, Design of Transition Metal/Main Group Elements Synergetic Reagent and Its Synthetic Application, Grant-in-Aid for Scientific Research on Priority Areas, 1 April 2006–31 March 2009.

Nakamura M, Exploratory Study on New Chemical Reactions Exploiting Biorenewable Carbon Resources, Kyoto University, ISS (Institute for Sustainability Science) Research Grant for Exploratory Studies, 1 April 2006–31 March 2008.

Hatakeyama T, Development of SN_2 Reaction of Carbon–Heteroatom Bond with Highly Reactive Metal Enolate, Grant-in-Aid for Young Scientists (Start), 1 April

Unsymmetrical Biaryl Syntheses

Transition metal-catalyzed cross-coupling reactions are one of the most powerful tools in organic synthesis. Palladium and nickel catalysts have been the dominant choice for such a purpose, and are widely used in academia as well as in industry. Whereas iron, a practically ideal transition metal, has been actively investigated as a catalyst in the field of cross-coupling reactions, iron-catalyzed aryl-aryl cross-coupling has remained a challenge because of competing homo-coupling reaction caused by oxidation with organic halides or iron-catalyzed halogen-metal exchange. We found a simple and highly selective iron-catalyzed cross-coupling reaction which selectively produced unsymmetrical biaryl compounds (Figure 1). The key to success is a novel combination of iron fluoride salts with an *N*-heterocyclic carbene (NHC) ligand, which specifically suppressed homo-coupling reactions (1–5% in most cases).

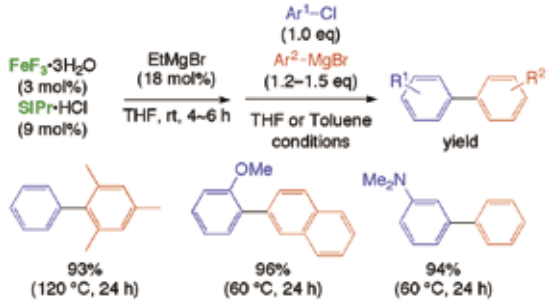

Figure 1. Selective Biaryl Cross-Coupling.

Cross-Coupling of Alkyl Tosylate

We sometime ago developed a new iron-catalyzed cross-coupling reaction of alkyl halides with aryl magnesium or zinc compounds in the presence of *N*, *N*, *N'*, *N'*-tetramethylethylenediamine (TMEDA). Whereas the alkyl halides are industrial feedstock and produced from corresponding alcohols, their preparative conditions are strongly acidic, and thus the overall yields are often low for certain substrates with functionalities. Cross-coupling of alkyl tosylates or triflates is, hence, more feasible and useful for the synthesis of fine chemicals. We found $FeCl_3$/TMEDA catalyst effect the cross-coupling of alkyl tosylates in the presence of zinc iodide, which converts *in-situ* the alkyl tosylates to corresponding iodides. With this one-pod method various secondary alkyl tosylates and arylzinc reagents possessing a variety of functional groups are available for the selective cross-coupling.

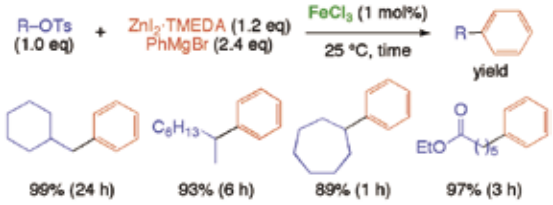

Figure 2. Cross-Coupling of Alkyl Tosylate.

Fluoroaromatic Coupling of Alkyl Halides

Fluoroaromatic rings are found as a key structural unit of numerous functional molecules, such as liquid crystals, drugs, agrochemicals, and dyes. Recent progress in the cross-coupling technology provided numbers of powerful methods for connecting fluoroaromatic rings with unsaturated (Csp^2 or Csp) substituents, but nonetheless few for introducing alkyl (Csp^3) substituents. Despite the fact that various cross-couplings of alkyl electrophiles and arylmetallic nucleophiles have been achieved, only a few fluoroaromatic couplings are available because of the low reactivity and instablity (e.g. undesired Csp^2-F bond cleavage) of polyfluorinated aryl metals under the reaction conditions. We have developed an effective and selective fluoroaromatic coupling of alkyl halides, which has been accomplished by combination of easily available fluoroaromatic metal reagents and 1,2-bis(diphenylphosphino)b enzene (DPPBz) as a ligand. The reaction can provide a concise synthetic route for the production of LC molecules (Figure 3).

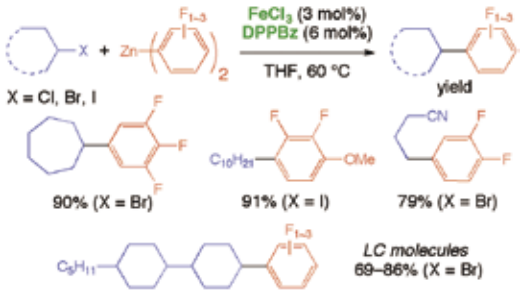

Figure 3. Fluoroaromatic Coupling of Alkyl Halides.

2006–31 March 2007.

Hatakeyama T, Refined Transformation of Biomass via S_N2 Reaction of Carbon–Heteroatom, Grant-in-Aid for Young Scientists (B), 1 April 2007–31 March 2009.

Award

Hatakeyama T, The ICR Award for Young Scientists, 7 December 2007.